Notice of Allowability	Application No.	Applicant(s)	
	09/823,257	LANDERS, JOHN E.	
	Examiner	Art Unit	
	Jeanine A Goldberg	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *6/1/04*.

2. ☒ The allowed claim(s) is/are *1,4-10,12-22,25-27 and 65*.

3. ☒ The drawings filed on *11 January 2002* are accepted by the Examiner.

4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☐ All b) ☐ Some* c) ☐ None of the:
      1. ☐ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

6. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

7. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☐ Information Disclosure Statements (PTO-1449 or PTO/SB/08), Paper No./Mail Date _____
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application (PTO-152)
6. ☒ Interview Summary (PTO-413), Paper No./Mail Date *8/04* .
7. ☒ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

DETAILED ACTION

1. This action is in response to the papers filed June 1, 2004.

EXAMINER'S AMENDMENT

2. An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

3. Authorization for this examiner's amendment was given in a telephone interview with Helen Lockhart on August 5 and August 6, 2004.

4. The application has been amended as follows:

A) Claims 3 and 11 have been cancelled without prejudice or disclaimer.

B) Claim 4 has been amended to recite - - The method of Claim 1, wherein a first ASO complementary to a first allele of the first SNP and a second ASO complementary to a second allele of the first SNP are fixed to the surface and are used to capture the nucleic acid. - -

C) Claims 12 and 13 have been amended to depend on Claim 1.

5. The following is an examiner's statement of reasons for allowance.

The claims are drawn to methods of haplotyping by analyzing a first polymorphic locus of a nucleic acid within a sample by specifically capturing the nucleic acid on a

surface wherein the step of capturing the nucleic acid on the surface identifies only a first allele of a first SNP of the polymorphic locus; analyzing a second allele of the first SNP of the polymorphic locus by specifically capturing the nucleic acid on a surface wherein the step of capturing the nucleic acid on the surface identifies only the second allele of the first SNP of the polymorphic locus, where the nucleic acid is captured by hybridization with an ASO, separately analyzing a second SNP of a polymorphic locus of the captured nucleic acid by hybridization of the nucleic acids with labeled ASOs from solution to identify both alleles of the second SNP, and determining the haplotype based on the identification of each allele of each SNP. The prior art fails to specifically teach or suggest all of the limitations of the instant claims.

Specifically, Gentalen teaches a method of using an array of probes in genetic analysis which use multiple cells in an array containing different pooled mixtures of probes. Gentalen provides an example which detects a target nucleic acid having two polymorphic sites, each of which has two polymorphic forms (A/a and B/b). Four combinations of the probes exist (AB, aB, ab, Ab). The target sequence is analyzed by designing four cells each containing a different pool of two mixed probes. The pool of probes having both component probes matched with the target nucleic acid shows the highest binding (col. 9, lines 40-55). Gentalen does not teach analyzing a second SNP of a polymorphic locus using labeled ASOs from solution, as required by the instant claims. All of Gentalen's probes are immobilized. While performing the entire assay in solution may have been obvious, there is no motivation to remove only a single immobilized probe such that a sandwich like assay is formed.

Arnold teaches methods of detecting single nucleotide polymorphisms (SNPs) by capturing probes which contain different labels. Arnold provides an example for simultaneously probing for n different SNPs on a target with m alleles each exploits n x m differentially detectable labels. For example, for two SNPs each with two alleles, this embodiment exploit four differentially detectable labels measures as for instance, a Cy2/Cy7 ration for one SNP and a Cy3/Cy5 for the second SNP (col. 5, lines 35-45). Arnold does not specifically teach capturing using an ASO probe on the solid support, as required by the instant claims. Arnold specifically contemplates using an array element linker on the substrate to capture the nucleic acid and then detecting a SNP using a detector probe. Adding the element of an ASO specific capture probe would not have been obvious given the teachings in the art and further the art teaches no motivation for performing such a method.

Finally, Dapprich teaches a method for isolating nucleic acids using targeting elements in a molecule that binds specifically to a nucleic acid sequence in a population (page 2, lines 22-24). The targeting element is used to bind to a target nucleic acid sequence for detecting a distinguishing element (page 2, lines 31-33). The targeting element with the attached separation group may be immobilized to a substrate forming an immobilized targeting element-separation group complex for at least one nucleic acid sequence (page 4, lines 25-30). Dapprich suggests a method of analyzing haplotypes, however, the methods do not teach or suggest the instantly claimed methods because Dapprich fails to suggest a method of capturing at a first locus followed by ASO in solution. The multiplex analysis of multiple SNPs discussed by Dapprich is directed to

using separation elements such as biotinylated "a" and a distinct separation element of fluorescein-modified "C". Dapprich does not specifically teach detecting the second SNP on the same captured nucleic acid (see Figure 11), as required by the instant claims.

Therefore, since the art neither teaches nor fairly suggests all of the limitations of the instant claims, the claims are allowable over the art.

6. Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jeanine Goldberg whose telephone number is (571) 272-0743. The examiner can normally be reached Monday-Friday from 7:00 a.m. to 4:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion, can be reached on (571) 272-0782.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

J. Goldberg

Jeanine Goldberg
Patent Examiner
August 6, 2004